# General

## Guideline Title

ACR Appropriateness Criteria® incidentally discovered adrenal mass.

## Bibliographic Source(s)

Remer EM, Casalino DD, Bishoff JT, Coursey CA, Dighe M, Eberhardt SC, Goldfarb S, Harvin HJ, Lazarus E, Leyendecker JR, Lockhart ME, Majd M, Nikolaidis P, Oto A, Porter C, Ramchandani P, Sheth S, Vikram R, Expert Panel on Urologic Imaging. ACR Appropriateness CriteriaÂ® incidentally discovered adrenal mass. [online publication]. Reston (VA): American College of Radiology (ACR); 2012. 10 p. [74 references]

## Guideline Status

This is the current release of the guideline.

This guideline updates a previous version: Francis IR, Casalino DD, Arellano RS, Baumgarten DA, Curry NS, Dighe M, Fulgham P, Israel GM, Leyendecker JR, Papanicolaou N, Prasad S, Ramchandani P, Remer EM, Sheth S, Expert Panel on Urologic Imaging. ACR Appropriateness Criteria® incidentally discovered adrenal mass. [online publication]. Reston (VA): American College of Radiology (ACR); 2009. 8 p.

# Recommendations

## Major Recommendations

ACR Appropriateness Criteria®

Clinical Condition: Incidentally Discovered Adrenal Mass

Variant 1: No history of malignancy; mass 1 to 4 cm in diameter. Initial evaluation.

| Radiologic Procedure | Rating | Comments | RRL* |
|---|---|---|---|
| CT abdomen without contrast | 8 | Presumes that a noncontrast CT has not already been performed and that there are no suspicious imaging features. Should be evaluated by radiologist to determine if contrast administration is needed. | |
| CT abdomen without and with contrast | 8 | Indicated if noncontrast CT is not diagnostic or if there are concerning imaging features of malignancy. Delayed imaging obtained to calculate washout. | |

Rating Scale: 1,2,3 Usually not appropriate; 4,5,6 May be appropriate; 7,8,9 Usually appropriate

*Relative Radiation Level

| Radiologic Procedure | Rating | Comments | RRL* |
|---|---|---|---|
| MRI abdomen without contrast | 8 | May be helpful when nonenhanced CT is equivocal or if there are suspicious imaging features. Appropriate for patient with iodinated contrast allergy. | O |
| MIBG | 2 | Only for suspicion of pheochromocytoma. | |
| MRI abdomen without and with contrast | 2 | | O |
| US adrenal gland | 1 | | O |
| Biopsy adrenal gland | 1 | | Varies |
| CT abdomen with contrast | 1 | | |
| X-ray abdomen | 1 | | |
| Iodocholesterol scan | 1 | This agent may be used to detect functionally active adenomas. | |
| FDG-PET/CT skull base to mid-thigh | 1 | | |
| Rating Scale: 1,2,3 Usually not appropriate; 4,5,6 May be appropriate; 7,8,9 Usually appropriate | | | *Relative Radiation Level |

Note: Abbreviations used in the tables are listed at the end of the "Major Recommendations" field.

Variant 2: No history of malignancy; mass 1 to 4 cm in diameter. Follow-up evaluation for indeterminate lesion on initial evaluation.

| Radiologic Procedure | Rating | Comments | RRL* |
|---|---|---|---|
| CT abdomen without contrast | 8 | Alternative to MRI without contrast to assess for size change in 12 months. | |
| MRI abdomen without contrast | 8 | Alternative to CT without contrast to assess for size change in 12 months. | O |
| MRI abdomen without and with contrast | 1 | | O |
| CT abdomen with contrast | 1 | Contrast unnecessary to assess for size change. | |
| CT abdomen without and with contrast | 1 | | |
| Rating Scale: 1,2,3 Usually not appropriate; 4,5,6 May be appropriate; 7,8,9 Usually appropriate | | | *Relative Radiation |

| Radiologic Procedure | Rating | Comments | RRL* |
|---|---|---|---|
| | | | |
| Rating Scale: 1,2,3 Usually not appropriate; 4,5,6 May be appropriate; 7,8,9 Usually appropriate | | | *Relative Radiation Level |

Note: Abbreviations used in the table are listed at the end of the "Major Recommendations" field.

Variant 3: No history of malignancy; mass >4 cm in diameter. (If not typical for adenoma, myelolipoma, hemorrhage, or simple cyst, consider resection.)

| Radiologic Procedure | Rating | Comments | RRL* |
|---|---|---|---|
| CT abdomen with contrast | 8 | As part of preoperative staging. Alternative to MRI. | |
| MRI abdomen without and with contrast | 8 | As part of preoperative staging. Alternative to CT. See statement regarding contrast in text under "Anticipated Exceptions." | O |
| FDG-PET/CT skull base to mid-thigh | 5 | As part of preoperative staging. | |
| MIBG | 2 | Only for suspicion of pheochromocytoma. | |
| CT abdomen without and with contrast | 2 | | |
| MRI abdomen without contrast | 1 | | O |
| US adrenal gland | 1 | | O |
| CT abdomen without contrast | 1 | | |
| X-ray abdomen | 1 | | |
| Iodocholesterol scan | 1 | This agent may be used to detect functionally active adenomas. | |
| Biopsy adrenal gland | 1 | | Varies |
| Rating Scale: 1,2,3 Usually not appropriate; 4,5,6 May be appropriate; 7,8,9 Usually appropriate | | | *Relative Radiation Level |

Note: Abbreviations used in the table are listed at the end of the "Major Recommendations" field.

Variant 4: History of malignancy; mass <4 cm in diameter. Initial evaluation.

| Radiologic Procedure | Rating | Comments | RRL* |
|---|---|---|---|
| CT abdomen without contrast | 8 | Should be evaluated by radiologist to determine if contrast administration is needed. | |
| CT abdomen without and with contrast | 8 | Indicated if noncontrast CT is indeterminate (attenuation >10 HU) or lesion does not lose signal on out-of-phase images. Delayed imaging obtained to calculate washout. | |
| MRI abdomen without contrast | 8 | Alternative to CT without contrast. | O |
| FDG-PET/CT skull base to mid-thigh | 8 | Alternative to CT and MRI. | |
| Biopsy adrenal gland | 5 | A biopsy should only be performed for mass with suspicious imaging characteristics that cannot be characterized as benign and if pheochromocytoma is excluded. CT or US guidance could be used. | Varies |
| MIBG | 2 | Only for suspicion of pheochromocytoma. | |
| MRI abdomen without and with contrast | 1 | | O |
| US adrenal gland | 1 | | O |
| CT abdomen with contrast | 1 | | |
| X-ray abdomen | 1 | | |
| Iodocholesterol scan | 1 | This agent may be used to detect functionally active adenomas. | |
| Rating Scale: 1,2,3 Usually not appropriate; 4,5,6 May be appropriate; 7,8,9 Usually appropriate | | | *Relative Radiation Level |

Note: Abbreviations used in the table are listed at the end of the "Major Recommendations" field.

Variant 5: History of malignancy; mass >4 cm in diameter.

| Radiologic Procedure | Rating | Comments | RRL* |
|---|---|---|---|
| Rating Scale: 1,2,3 Usually not appropriate; 4,5,6 May be appropriate; 7,8,9 Usually appropriate | | | *Relative |
| Biopsy adrenal gland | 8 | | Varies |

| Radiologic Procedure | Rating | Comments | RRL* |
|---|---|---|---|
| FDG-PET/CT skull base to mid-thigh | 8 | Alternative to biopsy to diagnose metastasis. | |
| | | | |
| MRI abdomen without and with contrast | 1 | | O |
| MRI abdomen without contrast | 1 | | O |
| US adrenal gland | 1 | | O |
| CT abdomen with contrast | 1 | | |
| CT abdomen without contrast | 1 | | |
| MIBG | 1 | | |
| X-ray abdomen | 1 | | |
| CT abdomen without and with contrast | 1 | | |
| Iodocholesterol scan | 1 | | |
| Rating Scale: 1,2,3 Usually not appropriate; 4,5,6 May be appropriate; 7,8,9 Usually appropriate | | | *Relative Radiation Level |

Note: Abbreviations used in the table are listed at the end of the "Major Recommendations" field.

Summary of Literature Review

Introduction/Background

The adrenal "incidentaloma" is an unsuspected and asymptomatic mass, usually detected on computed tomography (CT) obtained for other purposes. Incidentally discovered adrenal masses can be of varying sizes, but in general, the larger the lesion the more likely it is to be symptomatic. The majority of incidentalomas are benign and most are adenomas. The prevalence of adenomas in the general population, as summarized by one group of researchers, ranges from 1% to 2%, although autopsy studies have shown rates as high as 6.6% to 8.7% depending on the age distribution of the patient sample. The risk of primary adrenal cortical carcinoma in this population is quite small, on the order of 0.06%; however, among patients with adrenal masses the risk is reported to be as high as 4.7%. Other adrenal malignancies include angiosarcoma, lymphoma, and pheochromocytoma. These are diminishingly rare in the general population.

Metastatic disease without a known history of primary malignancy is also unusual. In a recent study of 1,049 incidental adrenal masses in patients with no known history of cancer, none were malignant. The majority of lesions were adrenal adenomas, myelolipomas and cysts.

An incidental adrenal mass that is a metastasis in a patient who has no known primary malignancy is unusual. The situation is different for patients with a known history of malignancy. In this setting, the rate of metastatic disease has been reported to be as high as 25% to 72% depending on the size and type of the primary lesion. For instance, bronchogenic and renal carcinomas and melanoma have a relatively higher rate of adrenal metastases than other epithelial malignancies. Despite this, a report found that even in patients with non-small cell lung cancer, adenomas were more common than metastases.

The guidelines suggested here apply to masses detected incidentally during CT, ultrasound (US), or magnetic resonance imaging (MRI) evaluation. The patient may be free of symptoms, although the mass may later prove to be functional (i.e., Cushing's or Conn's adenoma or pheochromocytoma). The appropriateness of performing additional studies to ascertain whether the mass is more likely benign or malignant is discussed here.

Size

Size is an important variable in predicting malignancy of an incidentally discovered adrenal mass. Smaller lesions are usually benign. Conversely, larger lesions are often malignant. However, it is important to distinguish between populations with and without a history of malignancy. When considering size, however, it is important to distinguish between populations with and without a history of malignancy. One group of researchers studied 342 patients without a history of malignancy and found that the rate of malignancy in adrenal modules was only 1.5% and that all malignant lesions were >5 cm. In a series of 887 patients who had adrenal incidentalomas, a diameter >4 cm was shown to have 90% sensitivity for the detection of adrenocortical carcinoma but low specificity; only 24% of lesions >4 cm in diameter were malignant.

In contrast, in patients with a history of malignancy, a group of authors found that 87% of lesions <3 cm were benign and that more than 95% of lesions >3 cm were malignant. In a similar population, another group found that 79% of lesions <2.5 cm were benign. Another study in a mixed population showed that a threshold of 3.1 cm discriminated 93% of lesions. Overall, size is considered too unreliable to be used alone as a criterion for malignancy, although in general a 4 cm cut-off is currently used to make decisions regarding surgery for lesions that do not have diagnostic imaging features such as can be seen in myelolipoma. While only approximately 6% of lesions between 4 and 6 cm are malignant, adrenalectomy is often recommended for individuals who are at acceptable risk for surgery. Masses ≥6 cm are resected, since the malignancy rate in this patient group is reported to exceed 25%. These recommendations are supported by a review of adrenal carcinoma that included 4,275 patients from the National Cancer database. The review showed that only 16% of all carcinomas and 18.2% of localized carcinomas were <6 cm, while 91.1% of all masses and 89.5% of localized masses were >4 cm.

Interval growth of adrenal masses has also been advocated as a potential indicator of malignancy. There is, however, scant information on what size change over what time interval requires further investigation. A group of investigators found that a growth of 0.8 cm on follow-up CT had the highest combination of sensitivity (72%) and specificity (81%) when evaluating absolute size change, growth rate, and growth percent in 111 benign and 25 malignant pathologically proven adrenal lesions. While the unadjusted odds ratio for this threshold was 11.02, no threshold was found with 100% sensitivity or specificity.

Endocrinologic Function

Even though incidentally discovered adrenal masses are by definition asymptomatic, a proportion will show subclinical function. One group of researchers found that 23% of patients who had an adrenal mass but no history of malignancy had detectable secretion of aldosterone, cortisol, or catecholamines. A similar study found that percentage to be 12%. Routine endocrinologic screening of patients with incidentalomas has been recommended. The Swedish Cooperative Study of 388 patients with adrenal incidentalomas found that 5% of them were hypersecreting and included pheochromocytomas (70%) and functional cortical adenomas (30%). A follow-up Swedish study performed in 187 patients without malignancy, evaluated outside of a specialized endocrinological group, found hormonally active tumors in 3%. Further, all patients with primary hyperaldosteronism or catecholamine-producing tumors had clinically evident disease at the primary evaluation. Thus, testing for subclinical hyperfunction may be warranted in selected cases. Supporting this practice, two recent series have found a much higher percentage of pheochromocytomas discovered incidentally (29% to 59%) than previous studies suggest.

Computed Tomography

CT not only detects incidentally discovered adrenal masses but also offers one of the best means of differentiating the benign from the malignant masses. There are no data on CT accuracy in characterizing adrenal masses <1 cm. Anecdotally, many believe that masses <1cm do not require imaging workup because most are believed to be adenomas. Based on their imaging features, some benign lesions such as cysts and myelolipomas are readily characterized by CT. Adrenal adenomas contain lipid to varying degrees, and this lowers their attenuation coefficient on noncontrast-enhanced CT. One group of researchers showed that when 0 Hounsfield units (HU) was used as a threshold value, the sensitivity for adenomas was 48% without any false positives. If the threshold was increased to 10 HU, the sensitivity was 56% with a 4% false positive rate. This has been confirmed by another study; however, another study found that no false positives were seen up to a threshold of 16.5 HU. One group has shown that there is some variability in the density measurements on different CT scanners. A threshold value of 10 HU is generally accepted as a cut-off

value for diagnosing a lipid-rich adenoma, as the 10 HU threshold has a 71% sensitivity and specificity of 98% for adenomas in a summary analysis of seven studies.

Another study has demonstrated that using histograms of pixel values rather than the average value of the region of interest allows more adenomas to be identified while preserving a high specificity. If 5% or more of the pixels of a lesion are less than 0 HU, the lesion is very likely to be an adenoma. This is of particular relevance when a contrast agent has been administered. Although sensitivity is reduced compared to nonenhanced CT, the use of histogram analysis can improve the sensitivity for adenoma from 10% to 36% if >5% of pixels are negative. However, another study of 208 pathologically proven adrenal masses showed that negative pixels were seen in metastases, adrenal carcinomas, and pheochromocytomas. In addition, the authors noted that using a 5% negative pixel threshold improved specificity for adenoma diagnosis; however, the low sensitivity precluded clinical usefulness. A group of researchers has recently shown that histogram analysis is superior to density measurements for the diagnosis of lipid-poor adenomas on unenhanced CT, with 51.6% of 31 lipid-poor adenomas having >10% negative pixels with no false positives (specificity 100%). A prospective study showed that using a 10% negative pixel threshold has a higher sensitivity than the ≤10 HU mean attenuation threshold method to discriminate adenomas from nonadenomas on unenhanced CT while maintaining a 100% specificity.

Unenhanced CT is a relatively inexpensive yet highly specific test for differentiating adenomas and some benign nonadenomas from malignant lesions. One group of researchers has shown that delayed enhanced CT and use of washout percentages are better able to distinguish adenomas from metastases than unenhanced CT alone. Both lipid-rich and lipid-poor adenomas tend to wash out faster after administration of intravenous contrast. This may result from the increased "leakiness" of malignant vessels compared with benign lesions. These researchers also showed that following a delay of 15 minutes after the administration of intravenous contrast, the sensitivity and specificity of CT could be greatly improved (sensitivity >95%, specificity >97%). Another study had similar results using 30-minute delay times (sensitivity 97%, specificity 100%). The accuracy of washout values was validated in another study of 166 adrenal masses, accurate characterization being achieved in 96% of masses. Thus, this technique is the main tool that is used at many institutions for distinguishing between adenomas and nonadenomas and is superior to nonenhanced CT.

Magnetic Resonance Imaging

Qualitative and quantitative MRI methods have been used to attempt to distinguish between adenomas and nonadenomas. MRI with chemical-shift (in and opposed phase) imaging (CSI), introduced by Leroy-Willig et al in 1989, relies on differentiating lesions by their relative lipid content, malignant lesions having virtually no lipid. Another study showed that CSI was correct in 96% of cases, and another study showed that the technique was 100% correct when using a slight variation. Unfortunately, all of these studies were performed in a mixed population of patients with regard to the history of malignancy, so results may not be directly applicable to populations either with or without known malignancy (patient mix will greatly influence results).

Since then, several authors have shown excellent results in a relevant population using simpler CSI techniques. Analytic approaches have also varied from simple visual assessment of signal loss on out-of-phase (OOP) imaging compared to in-phase (IP) imaging to quantitative measures of signal loss. One group of researchers concluded that a signal intensity index (IP-OOP/IP) was superior to other methods that normalized signal to spleen, liver, or muscle.

Another study demonstrated substantial advantages to applying CSI imaging in cases where the CT density measurement was between 10 and 30 HU (i.e., indeterminate by CT). For instance, in adenomas with densities between 10 and 30 HU, 89% of the lesions were correctly characterized by CSI. Similar results have been obtained by another group, who concluded that up to 60% of lesions misclassified by unenhanced CT density measurements can be correctly characterized as adenomas by chemical-shift MRI. One other study has demonstrated that even heterogeneous loss of signal is evidence of a benign lesion. Thus, chemical-shift MRI may have better sensitivity and specificity than nonenhanced CT. However, in another study with a small sample size that compared delayed enhanced CT and chemical-shift MRI, the authors showed that delayed enhanced CT was slightly superior to chemical-shift MR in characterizing adrenal masses measuring more than 10 HU on unenhanced CT. A prospective study found a higher sensitivity to adenoma with CSI (97%) using an adrenal-to-spleen chemical-shift ratio of less than 0.71 compared to 91% for CT histogram analysis using a 10% negative pixel threshold on unenhanced scans, each with 100% specificity.

Diffusion-weighted MRI techniques have recently been used to help distinguish benign and malignant masses in various organ systems. Two studies found that this technique could not help differentiate adrenal adenomas and nonadenomas.

Adrenal Biopsy

Biopsy of the incidental adrenal mass has been performed under CT guidance for over 25 years. Most studies on the efficacy of adrenal biopsy have been performed in a mixed population of patients. Biopsy samples insufficient to make a diagnosis are obtained in 4% to 19% (mean = 15%) of cases. When sufficient material is obtained, the accuracy of biopsy is 96% to 100% for malignant lesions. Biopsy interpretation is more difficult

in benign processes. Fine needle aspiration alone cannot be used to differentiate adrenocortical carcinoma from adrenal adenoma. Careful correlation with clinical and endocrinological data is needed, combined with a knowledge of other features such as tumor size and imaging characteristics to distinguish adenoma from carcinoma due to the possibility of sampling error. Thus, biopsy is better suited to a population with a high risk of malignant lesions and is most useful when noninvasive studies are negative or inconclusive. The role of adrenal biopsy has evolved, and it is now performed to exclude the presence of metastases when noninvasive tests are inconclusive, or when enlarging adrenal masses are seen at follow-up imaging, or to confirm the presence of an adrenal metastasis. Complication rates range from 8% to 12% and consist of bleeding, pneumothorax, infection, and anecdotes of tumor tracking. Several deaths have been reported after an adrenal biopsy of a pheochromocytoma. One group of researchers demonstrated that when biopsy was compared to CT and MRI it had the highest combination of sensitivity and specificity (83% and 100%, respectively).

Radionuclide Studies

Iodocholesterol (NP 59) scans are rarely used in the United States and are confined to a few major centers. NP 59 studies will detect any lesion with functioning adrenal tissue. Thus, hyperfunctional adenomas (Conn's and Cushing's adenomas) and many nonhyperfunctioning adenomas will bind this agent. When the CT and NP 59 scan are concordant, the lesion is benign in all cases. One group of researchers studying a population of patients with a history of tumor showed that most (82%) lesions with discordant uptake were metastatic; 11% were indeterminate. Thus, radionuclide studies are very useful if concordant but overlap significantly if they are discordant with the CT findings.

Metaiodobenzylguanidine (MIBG) studies are useful in patients suspected of a pheochromocytoma, but this is rarely the case in the incidentally detected adrenal mass.

Fluorine-18-2-fluoro-2-deoxy-D-glucose (FDG)-labeled for positron emission tomography (PET) can be used to identify metastases in oncologic patients with various cancers. FDG-PET is sensitive to metabolically active lesions, and metastases usually show greater uptake than benign lesions. In several studies, there have been few false positives with FDG-PET, lowering specificity to 85% in one study, but excellent sensitivity has been achieved. False negative scans have occurred in renal cell carcinoma metastases.

Specific uptake values (SUVs) are typically greater for metastatic disease. However, mild activity can be seen in benign adenomas, thus leading to false positive interpretations. Studies have predominantly evaluated FDG-PET or PET/CT in the oncologic population. A group of authors evaluated 41 adrenal tumors in 37 patients who had no history of malignancy using FDG-PET/CT. All tumors were without diagnostically benign features on CT or MRI. In this small series, a tumor/liver $SUV_{max}$ ratio >1.8, yielded 100% sensitivity and specificity for malignancy. Recently, a new tracer for PET, 11C-metomidate, has been found to localize in adrenocortical tumors, and it is useful for determining whether a tumor is of adrenocortical origin. However, it cannot distinguish between benign and malignant tumors.

Summary

- For patients with no history of malignancy, most small (<4 cm) incidentally discovered adrenal masses are benign, and an extensive and costly workup is usually not justified. If a mass of any size has typical features of a benign lesion such as a lipid-rich adenoma or myelolipoma, no additional workup or follow-up imaging is needed. In those with nondiagnostic imaging features, if prior imaging is available and the lesion is stable for at least 1 year, it can be deemed benign with no additional imaging follow-up. While a specific size change threshold is unknown, if the lesion is enlarging, then it may be prudent to proceed to an adrenal biopsy or resection.
- If there is no prior CT or MRI examination for comparison, and if the lesion has benign imaging features on routine postcontrast CT but no unenhanced CT or adrenal-specific imaging is available, a diagnosis of a benign lesion can be presumed, and one may consider a follow-up unenhanced CT or CSI examination in 12 months. However, if there are suspicious imaging features, then one should proceed with an unenhanced CT or CSI and from there proceed to an adrenal CT protocol with washout calculations if needed. If the lesion does not have imaging and washout features of a benign lesion, then a biopsy should be considered.
- If there is a history of malignancy and imaging features are not diagnostic for a benign lesion and no prior imaging is available, one can consider PET imaging or an unenhanced CT or CSI. If the lesion does not behave like a typical adenoma, then one should proceed to adrenal CT with washout. If the lesion does not show washout features of an adenoma or findings of an adenoma on PET imaging, then a biopsy is warranted.
- In patients with no history of cancer and an adrenal mass >4 cm in size, one may consider resection. If there is a history of prior malignancy, however, one may consider a PET scan or a biopsy.
- Endocrinologic evaluation may be considered, as subclinical hyperfunction has been reported to be present in 5% of adrenal incidentalomas per the recommendations of the National Institutes of Health consensus conference on adrenal incidentalomas.
- Lesions >4 cm and not having imaging features diagnostic of benign lesions, such as adenoma or myelolipoma, are generally removed in most centers due to the higher risk of malignancy.
- For patients with a history of malignancy, it is important to exclude from further evaluation any patient with widespread nonadrenal metastases since, in this setting, the presence or absence of adrenal metastases is unlikely to influence the patient's outcome. An unenhanced

CT and, if needed, a delayed enhanced CT, can be used in this setting. If these cannot rule in an adenoma, FDG-PET, chemical-shift MRI, or biopsy should be considered. Adrenal biopsy should be reserved for cases where the noninvasive techniques are equivocal and to confirm the presence of metastases. In patients suspected of having a functional lesion, iodocholesterol, or 11C-metomidate or MIBG studies may be useful.

- Radiography and US have no role in characterizing adrenal lesions.

Anticipated Exceptions

Patients with pheochromocytoma should not have adrenal biopsy unless properly pretreated. This diagnosis should be excluded prior to biopsy with urinary or plasma catecholamine levels. In equivocal cases, a glucagon stimulation test should be done before biopsy of a potential pheochromocytoma.

Nephrogenic systemic fibrosis (NSF) is a disorder with a scleroderma-like presentation and a spectrum of manifestations that can range from limited clinical sequelae to fatality. It appears to be related to both underlying severe renal dysfunction and the administration of gadolinium-based contrast agents. It has occurred primarily in patients on dialysis, rarely in patients with very limited glomerular filtration rate (GFR) (i.e., <30 mL/min/1.73 $m^2$), and almost never in other patients. There is growing literature regarding NSF. Although some controversy and lack of clarity remain, there is a consensus that it is advisable to avoid all gadolinium-based contrast agents in dialysis-dependent patients unless the possible benefits clearly outweigh the risk, and to limit the type and amount in patients with estimated GFR rates <30 mL/min/1.73 $m^2$. For more information, please see the American College of Radiology (ACR) Manual on Contrast Media (see the "Availability of Companion Documents" field).

Abbreviations

- CT, computed tomography
- FDG-PET, fluorine-18-2-fluoro-2-deoxy-D-glucose positron emission tomography
- HU, Hounsfield units
- MIBG, metaiodobenzylguanidine
- MRI, magnetic resonance imaging
- US, ultrasound

Relative Radiation Level Designations

| Relative Radiation Level* | Adult Effective Dose Estimate Range | Pediatric Effective Dose Estimate Range |
|---|---|---|
| O | 0 mSv | 0 mSv |
| | <0.1 mSv | <0.03 mSv |
| | 0.1-1 mSv | 0.03-0.3 mSv |
| | 1-10 mSv | 0.3-3 mSv |
| | 10-30 mSv | 3-10 mSv |
| | 30-100 mSv | 10-30 mSv |
| *RRL assignments for some of the examinations cannot be made, because the actual patient doses in these procedures vary as a function of a number of factors (e.g., region of the body exposed to ionizing radiation, the imaging guidance that is used). The RRLs for these examinations are designated as “Varies.” | | |

## Clinical Algorithm(s)

Algorithms were not developed from criteria guidelines.

# Scope

## Disease/Condition(s)

Adrenal mass

## Guideline Category

Diagnosis

Evaluation

## Clinical Specialty

Endocrinology

Internal Medicine

Nuclear Medicine

Oncology

Pathology

Radiology

## Intended Users

Health Plans

Hospitals

Managed Care Organizations

Physicians

Utilization Management

## Guideline Objective(s)

To evaluate the appropriateness of radiologic procedures for the evaluation of an incidentally discovered adrenal mass

## Target Population

Patients with adrenal mass

Note: The guidelines suggested here apply to masses detected incidentally during computed tomography, ultrasound, or magnetic resonance imaging evaluation.

## Interventions and Practices Considered

1. Computed tomography (CT) abdomen
    - With contrast
    - Without contrast
    - Without and with contrast
2. Magnetic resonance imaging (MRI) abdomen
    - Without contrast

    - Without and with contrast
3. Metaiodobenzylguanidine (MIBG)
4. Ultrasound (US) adrenal gland
5. Biopsy adrenal gland
6. X-ray abdomen
7. Iodocholesterol scan
8. Fluorine-18-2-fluoro-2-deoxy-D-glucose positron emission tomography (FDG-PET)/CT skull base to mid-thigh

### Major Outcomes Considered

Utility of radiologic procedures in the evaluation of patients with adrenal mass

## Methodology

### Methods Used to Collect/Select the Evidence

Searches of Electronic Databases

### Description of Methods Used to Collect/Select the Evidence

Literature Search Procedure

The Medline literature search is based on keywords provided by the topic author. The two general classes of keywords are those related to the condition (e.g., ankle pain, fever) and those that describe the diagnostic or therapeutic intervention of interest (e.g., mammography, MRI]).

The search terms and parameters are manipulated to produce the most relevant, current evidence to address the American College of Radiology Appropriateness Criteria (ACR AC) topic being reviewed or developed. Combining the clinical conditions and diagnostic modalities or therapeutic procedures narrows the search to be relevant to the topic. Exploding the term "diagnostic imaging" captures relevant results for diagnostic topics.

The following criteria/limits are used in the searches.

1. Articles that have abstracts available and are concerned with humans.
2. Restrict the search to the year prior to the last topic update or in some cases the author of the topic may specify which year range to use in the search. For new topics, the year range is restricted to the last 5 years unless the topic author provides other instructions.
3. May restrict the search to Adults only or Pediatrics only.
4. Articles consisting of only summaries or case reports are often excluded from final results.

The search strategy may be revised to improve the output as needed.

### Number of Source Documents

The total number of source documents identified as the result of the literature search is not known.

### Methods Used to Assess the Quality and Strength of the Evidence

Weighting According to a Rating Scheme (Scheme Given)

### Rating Scheme for the Strength of the Evidence

Strength of Evidence Key

Category 1 - The conclusions of the study are valid and strongly supported by study design, analysis, and results.

Category 2 - The conclusions of the study are likely valid, but study design does not permit certainty.

Category 3 - The conclusions of the study may be valid but the evidence supporting the conclusions is inconclusive or equivocal.

Category 4 - The conclusions of the study may not be valid because the evidence may not be reliable given the study design or analysis.

## Methods Used to Analyze the Evidence

Systematic Review with Evidence Tables

## Description of the Methods Used to Analyze the Evidence

The topic author drafts or revises the narrative text summarizing the evidence found in the literature. American College of Radiology (ACR) staff draft an evidence table based on the analysis of the selected literature. These tables rate the strength of the evidence for all articles included in the narrative text.

The expert panel reviews the narrative text, evidence table, and the supporting literature for each of the topic-variant combinations and assigns an appropriateness rating for each procedure listed in the table. Each individual panel member forms his/her own opinion based on his/her interpretation of the available evidence.

More information about the evidence table development process can be found in the ACR Appropriateness Criteria® Evidence Table Development document (see the "Availability of Companion Documents" field).

## Methods Used to Formulate the Recommendations

Expert Consensus (Delphi)

## Description of Methods Used to Formulate the Recommendations

Modified Delphi Technique

The appropriateness ratings for each of the procedures included in the Appropriateness Criteria topics are determined using a modified Delphi methodology. A series of surveys are conducted to elicit each panelist's expert interpretation of the evidence, based on the available data, regarding the appropriateness of an imaging or therapeutic procedure for a specific clinical scenario. American College of Radiology (ACR) staff distributes surveys to the panelists along with the evidence table and narrative. Each panelist interprets the available evidence and rates each procedure. The surveys are completed by panelists without consulting other panelists. The ratings are a scale between 1 and 9, which is further divided into three categories: 1, 2, or 3 is defined as "usually not appropriate"; 4, 5, or 6 is defined as "may be appropriate"; and 7, 8, or 9 is defined as "usually appropriate." Each panel member assigns one rating for each procedure per survey round. The surveys are collected and the results are tabulated, de-identified and redistributed after each round. A maximum of three rounds are conducted. The modified Delphi technique enables each panelist to express individual interpretations of the evidence and his or her expert opinion without excessive bias from fellow panelists in a simple, standardized and economical process.

Consensus among the panel members must be achieved to determine the final rating for each procedure. Consensus is defined as eighty percent (80%) agreement within a rating category. The final rating is determined by the median of all the ratings once consensus has been reached. Up to three rating rounds are conducted to achieve consensus.

If consensus is not reached, the panel is convened by conference call. The strengths and weaknesses of each imaging procedure that has not reached consensus are discussed and a final rating is proposed. If the panelists on the call agree, the rating is accepted as the panel's consensus. The document is circulated to all the panelists to make the final determination. If consensus cannot be reached on the call or when the document is circulated, "No consensus" appears in the rating column and the reasons for this decision are added to the comment sections.

## Rating Scheme for the Strength of the Recommendations

Not applicable

## Cost Analysis

A formal cost analysis was not performed and published cost analyses were not reviewed.

## Method of Guideline Validation

Internal Peer Review

## Description of Method of Guideline Validation

Criteria developed by the Expert Panels are reviewed by the American College of Radiology (ACR) Committee on Appropriateness Criteria.

# Evidence Supporting the Recommendations

## Type of Evidence Supporting the Recommendations

The recommendations are based on analysis of the current literature and expert panel consensus.

# Benefits/Harms of Implementing the Guideline Recommendations

## Potential Benefits

Selection of appropriate radiologic imaging procedures for the evaluation of patients with incidentally discovered adrenal mass

## Potential Harms

- Complication rates of adrenal biopsy range from 8% to 12% and consist of bleeding, pneumothorax, infection, and anecdotes of tumor tracking. Several deaths have been reported after an adrenal biopsy of a pheochromocytoma.
- Fluorine-18-2-fluoro-2-deoxy-D-glucose positron emission tomography (FDG-PET) can render false positive and false negative results.

Gadolinium-based Contrast Agents

Nephrogenic systemic fibrosis (NSF) is a disorder with a scleroderma-like presentation and a spectrum of manifestations that can range from limited clinical sequelae to fatality. It appears to be related to both underlying severe renal dysfunction and the administration of gadolinium-based contrast agents. It has occurred primarily in patients on dialysis, rarely in patients with very limited glomerular filtration rate (GFR) (i.e., <30 mL/min/1.73 $m^2$), and almost never in other patients. Although some controversy and lack of clarity remain, there is a consensus that it is advisable to avoid all gadolinium-based contrast agents in dialysis-dependent patients unless the possible benefits clearly outweigh the risk, and to limit the type and amount in patients with estimated GFR rates <30 mL/min/1.73 $m^2$. For more information, please see the American College of Radiology (ACR) Manual on Contrast Media (see the "Availability of Companion Documents" field).

Relative Radiation Level (RRL)

Potential adverse health effects associated with radiation exposure are an important factor to consider when selecting the appropriate imaging procedure. Because there is a wide range of radiation exposures associated with different diagnostic procedures, a relative radiation level indication has been included for each imaging examination. The RRLs are based on effective dose, which is a radiation dose quantity that is used to estimate population total radiation risk associated with an imaging procedure. Patients in the pediatric age group are at inherently higher risk from exposure, both because of organ sensitivity and longer life expectancy (relevant to the long latency that appears to accompany radiation exposure). For these reasons, the RRL dose estimate ranges for pediatric examinations are lower as compared to those specified for adults. Additional information regarding radiation dose assessment for imaging examinations can be found in the ACR Appropriateness Criteria® Radiation Dose Assessment Introduction document (see the "Availability of Companion Documents" field).

# Contraindications

## Contraindications

Patients with pheochromocytoma should not have adrenal biopsy unless properly pretreated. This diagnosis should be excluded prior to biopsy with urinary or plasma catecholamine levels.

# Qualifying Statements

## Qualifying Statements

The American College of Radiology (ACR) Committee on Appropriateness Criteria and its expert panels have developed criteria for determining appropriate imaging examinations for diagnosis and treatment of specified medical condition(s). These criteria are intended to guide radiologists, radiation oncologists and referring physicians in making decisions regarding radiologic imaging and treatment. Generally, the complexity and severity of a patient's clinical condition should dictate the selection of appropriate imaging procedures or treatments. Only those examinations generally used for evaluation of the patient's condition are ranked. Other imaging studies necessary to evaluate other co-existent diseases or other medical consequences of this condition are not considered in this document. The availability of equipment or personnel may influence the selection of appropriate imaging procedures or treatments. Imaging techniques classified as investigational by the U.S. Food and Drug Administration (FDA) have not been considered in developing these criteria; however, study of new equipment and applications should be encouraged. The ultimate decision regarding the appropriateness of any specific radiologic examination or treatment must be made by the referring physician and radiologist in light of all the circumstances presented in an individual examination.

# Implementation of the Guideline

## Description of Implementation Strategy

An implementation strategy was not provided.

# Institute of Medicine (IOM) National Healthcare Quality Report Categories

## IOM Care Need

Getting Better

Staying Healthy

## IOM Domain

Effectiveness

# Identifying Information and Availability

## Bibliographic Source(s)

Remer EM, Casalino DD, Bishoff JT, Coursey CA, Dighe M, Eberhardt SC, Goldfarb S, Harvin HJ, Lazarus E, Leyendecker JR, Lockhart ME, Majd M, Nikolaidis P, Oto A, Porter C, Ramchandani P, Sheth S, Vikram R, Expert Panel on Urologic Imaging. ACR Appropriateness CriteriaÂ® incidentally discovered adrenal mass. [online publication]. Reston (VA): American College of Radiology (ACR); 2012. 10 p. [74 references]

## Adaptation

Not applicable: The guideline was not adapted from another source.

## Date Released

1996 (revised 2012)

## Guideline Developer(s)

American College of Radiology - Medical Specialty Society

## Source(s) of Funding

The American College of Radiology (ACR) provided the funding and the resources for these ACR Appropriateness Criteria®.

## Guideline Committee

Committee on Appropriateness Criteria, Expert Panel on Urologic Imaging

## Composition of Group That Authored the Guideline

*Panel Members*: Erick M. Remer, MD (*Principal Author and Panel Vice-chair*); David D. Casalino, MD (*Panel Chair*); Jay T. Bishoff, MD; Courtney A. Coursey, MD; Manjiri Dighe, MD; Steven C. Eberhardt, MD; Stanley Goldfarb, MD; Howard J. Harvin, MD; Elizabeth Lazarus, MD; John R. Leyendecker, MD; Mark E. Lockhart, MD, MPH; Massoud Majd, MD; Paul Nikolaidis, MD; Aytekin Oto, MD; Christopher Porter, MD; Parvati Ramchandani, MD; Sheila Sheth, MD; Raghunandan Vikram, MD

## Financial Disclosures/Conflicts of Interest

Not stated

## Guideline Status

This is the current release of the guideline.

This guideline updates a previous version: Francis IR, Casalino DD, Arellano RS, Baumgarten DA, Curry NS, Dighe M, Fulgham P, Israel GM, Leyendecker JR, Papanicolaou N, Prasad S, Ramchandani P, Remer EM, Sheth S, Expert Panel on Urologic Imaging. ACR Appropriateness Criteria® incidentally discovered adrenal mass. [online publication]. Reston (VA): American College of Radiology (ACR); 2009. 8 p.

## Guideline Availability

Electronic copies: Available from the American College of Radiology (ACR) Web site .

Print copies: Available from the American College of Radiology, 1891 Preston White Drive, Reston, VA 20191. Telephone: (703) 648-8900.

## Availability of Companion Documents

The following are available:

- ACR Appropriateness Criteria®. Overview. Reston (VA): American College of Radiology; 2 p. Electronic copies: Available in Portable Document Format (PDF) from the American College of Radiology (ACR) Web site.
- ACR Appropriateness Criteria®. Literature search process. Reston (VA): American College of Radiology; 1 p. Electronic copies: Available in PDF from the ACR Web site.
- ACR Appropriateness Criteria®. Evidence table development – diagnostic studies. Reston (VA): American College of Radiology; 2013 Nov. 3 p. Electronic copies: Available in PDF from the ACR Web site.
- ACR Appropriateness Criteria®. Radiation dose assessment introduction. Reston (VA): American College of Radiology; 2 p. Electronic copies: Available in PDF from the ACR Web site.
- ACR Appropriateness Criteria®. Manual on contrast media. Reston (VA): American College of Radiology; 90 p. Electronic copies: Available in PDF from the ACR Web site.
- ACR Appropriateness Criteria®. Procedure information. Reston (VA): American College of Radiology; 1 p. Electronic copies: Available in PDF from the ACR Web site.
- ACR Appropriateness Criteria® incidentally discovered adrenal mass. Evidence table. Reston (VA): American College of Radiology; 2012. 20 p. Electronic copies: Available in PDF from the ACR Web site.

## Patient Resources

None available

## NGC Status

This NGC summary was completed by ECRI on February 10, 2006. This NGC summary was updated by ECRI Institute on November 16, 2007. This NGC summary was updated by ECRI Institute on June 4, 2010. This NGC summary was updated by ECRI Institute on October 12, 2012.

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